



Complete Summary

GUIDELINE TITLE

Follow-up and retreatment of brain metastases.

BIBLIOGRAPHIC SOURCE(S)

Simpson JR, Gaspar LE, Aref AM, Imperato JP, Marcus KJ, Rogers CL, Suh JH, Videtic GM, Wolfson AH, McDermott MW, Rogers L, Expert Panel on Radiation Oncology-Brain Metastases. Follow-up and retreatment of brain metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [23 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Simpson JR, Mendenhall WM, Schupak KD, Larson D, Bloomer WD, Buckley JA, Gaspar LE, Gibbs FA, Lewin AA, Loeffler JS, Malcolm AW, Schneider JF, Shaw EG, Wharam MD Jr, Gutin PH, Rogers L, Leibel S. Follow-up and retreatment of brain metastases. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun;215(Suppl):1129-35.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

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SCOPE

DISEASE/CONDITION(S)

Brain metastases

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Neurological Surgery
Neurology
Oncology
Radiation Oncology
Radiology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of treatment procedures for follow-up and retreatment of patients with brain metastases

TARGET POPULATION

Patients requiring follow-up and retreatment of brain metastasis

INTERVENTIONS AND PRACTICES CONSIDERED

1. Local therapy
 - Surgical resection
 - Stereotactic radiosurgery (SRS)
2. Whole brain radiotherapy (WBRT)
3. Combined therapy
 - WBRT and radiosurgery
 - Surgery and postop WBRT
 - Surgery and postop radiosurgery
4. Chemotherapy
5. Observation
6. Follow-up
 - Magnetic resonance imaging (MRI), brain
 - Computed tomography (CT), brain
 - F-18 deoxyglucose positron emission tomography (FDG-PET)

MAJOR OUTCOMES CONSIDERED

- Morbidity or mortality

- Improved care
- Median survival time

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the appropriateness criteria. The American College of

Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. The modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Follow-up and Retreatment of Brain Metastasis

Variant 1: 70-year-old man with non-small-cell lung cancer s/p lobectomy 3 years ago with a single brain metastasis 1 year ago treated with radiosurgery. Now with new contralateral metastasis in non-dominant temporal lobe measuring 2 cm. KPS is 80.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	3	
Stereotactic radiosurgery (SRS)	7	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	2	
3000 cGy/10 fractions	7	
3750 cGy/15 fractions	7	
4000 cGy/20 fractions	2	
5000 cGy/25 fractions	2	
Combined Therapy		
WBRT and radiosurgery	8	
Surgery and postop WBRT	5	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	2	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 60-year-old man with renal cancer history, s/p surgical resection of two cerebellar metastases and postop WBRT (35 Gy in 14 fractions) 18 months ago. Now with new 3 cm left frontal metastasis without edema. KPS is 90. No other signs of recurrence.

Treatment	Appropriateness Rating	Comments
Local Therapy		

Treatment	Appropriateness Rating	Comments
Surgical resection	6	
Stereotactic radiosurgery (SRS)	8	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	1	
3000 cGy/10 fractions	2	
3750 cGy/15 fractions	2	
4000 cGy/20 fractions	2	
Combined Therapy		
WBRT and radiosurgery	2	
Surgery and postop WBRT	2	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	1	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 44-year-old woman with metastatic breast cancer and multiple brain metastases 9 months ago, s/p WBRT (3000 cGy in 10 fractions). Now with recurrence of 2 asymptomatic bilateral anterior frontal masses, 1-2 cm in diameter each. KPS is 80.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	3	
Stereotactic radiosurgery (SRS)	8	

Treatment	Appropriateness Rating	Comments
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	2	
3000 cGy/10 fractions	2	
3750 cGy/15 fractions	2	
4000 cGy/20 fractions	2	
Combined Therapy		
WBRT and radiosurgery	2	
Surgery and postop WBRT	2	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	2	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 49-year-old woman with widely metastatic melanoma, s/p WBRT (3000 cGy in 10 fractions) for multiple metastases 6 months ago. Now with recurrence of one 3.5 cm right parietal metastasis with edema causing weakness. KPS is 70.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	7	
Stereotactic radiosurgery (SRS)	7	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	2	

Treatment	Appropriateness Rating	Comments
3000 cGy/10 fractions	2	
3750 cGy/15 fractions	1	
4000 cGy/20 fractions	2	
Combined Therapy		
WBRT and radiosurgery	2	
Surgery and postop WBRT	2	
Surgery and postop radiosurgery	2	
Chemotherapy Alone	2	
Observation	2	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 76-year-old woman with a history of colon cancer 6 years ago and a single cerebellar metastasis 1 year ago, treated with WBRT (to 30 Gy in 10 fractions) and posterior fossa boost to 40 Gy. Now with new 2.5 cm right parietal lobe metastasis causing left-sided weakness. Posterior fossa lesion stable. KPS is 80. No other extracranial disease.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	7	
Stereotactic radiosurgery (SRS)	8	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	2	
3000 cGy/10 fractions	2	

Treatment	Appropriateness Rating	Comments
3750 cGy/15 fractions	2	
4000 cGy/20 fractions	2	
Combined Therapy		
WBRT and radiosurgery	2	
Surgery and postop WBRT	1	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	1	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: 62-year-old woman with recurrent ovarian cancer in the pelvis and metastases to the frontal and temporal lobes 1 year ago, treated with craniotomy for the larger frontal tumor and postoperative radiosurgery to both intracranial sites. Now with a new lateral cerebellar metastasis 2.8 cm in maximum diameter. Systemic disease is present and progressive over past 3 months. KPS is 60.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	2	
Stereotactic radiosurgery (SRS)	7	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	4	
3000 cGy/10 fractions	6	
3750 cGy/15 fractions	5	

Treatment	Appropriateness Rating	Comments
4000 cGy/20 fractions	2	
5000 cGy/25 fractions	2	
Combined Therapy		
WBRT and radiosurgery	3	
Surgery and postop WBRT	3	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	2	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: 37-year-old man with non-small-cell lung cancer and synchronous bilateral frontal metastases 8 months ago treated with radiosurgery only. Now with a new 4 cm parietal lobe metastasis affecting motor strength. There is progressive systemic disease. KPS is 70.

Treatment	Appropriateness Rating	Comments
Local Therapy		
Surgical resection	5	
Stereotactic radiosurgery (SRS)	4	
Whole Brain Radiotherapy (WBRT) Alone		
2000 cGy/5 fractions	3	
3000 cGy/10 fractions	7	
3750 cGy/15 fractions	7	
4000 cGy/20 fractions	2	

Treatment	Appropriateness Rating	Comments
5000 cGy/25 fractions	2	
Combined Therapy		
WBRT and radiosurgery	5	
Surgery and postop WBRT	6	
Surgery and postop radiosurgery	3	
Chemotherapy Only	2	
Observation	2	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: Follow-up after treatment of brain metastases. (Assuming in prior variants that treatment was carried out as planned, what is the frequency and modality of imaging in combination with a physical exam?).

Radiologic Procedure	Appropriateness Rating	Comments
MRI, brain		
≤3 months	7	
Every 4 months	7	
Every 6 months	5	
When symptomatic on physical exam only	4	
CT, brain		
Every 3 months	3	
Every 4 months	3	
Every 6 months	3	

Radiologic Procedure	Appropriateness Rating	Comments
FDG-PET, brain		
Every 3 months	2	
Every 4 months	2	
Only if MRI or CT abnormality suggests recurrence after radiosurgery or WBRT	6	
<i>Appropriateness Criteria Scale</i> 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Retreatment for brain metastases may be required following a variety of initial treatments such as whole brain irradiation, surgery, radiosurgery, chemotherapy, and combinations of these. The choice of recurrent treatment modality will depend on the size, number, timing, and location of the recurrent metastases as well as the patient's performance status and extent of extra central nervous system (CNS) disease beyond the central nervous system. There appears to be an increasing number of patients who have received only surgery or radiosurgery as their initial management of brain metastases. This trend is likely driven by the increasing availability of stereotactic radiosurgery, improvements in neuroimaging and surgical techniques, and patient desires for quality of life choices in health care.

Whole brain irradiation (WBRT) may be the least attractive option for retreatment after initial WBRT, although some authors dispute this. Less response is usually seen than with the first course, it is usually transient, and patients' morbidity is high if they survive long enough. Panel members consistently deemed whole brain reirradiation a less appropriate choice than the other alternatives.

Radiosurgery for recurrent brain metastases is a viable option if size and number permit. One study reported 1 and 2 years local control rates of 91% and 84% respectively, in 54 consecutive patients with radiosurgery for reirradiation of brain metastases following initial WBRT. Radiographic responses have been well documented for salvage radiosurgery, although evidence for a survival benefit is not strong. This modality is increasingly available at many centers.

Chemotherapy has occasionally been a successful strategy for chemosensitive tumors, whereas repeat surgery may be useful depending on patient condition.

Increasing evidence shows that some chemotherapy and biological treatments may be effective in brain metastases.

Follow-up of Brain Metastases

The best method of follow-up of brain metastases after treatment is complicated by the lack of reliable early indicators of response or progression. One study reported on the imaging changes after stereotactic radiosurgery of primary and secondary malignant brain tumors, finding that 22% of 35 metastatic tumors appeared larger on magnetic resonance imaging (MRI) at a mean of 10 weeks after radiosurgery. Eleven had fluorodeoxyglucose positron emission tomography (FDG-PET) performed for enlarging lesions -- eight showed increased brain activity, while three showed decreased activity. Of the eight, however, six were incorrectly predicted based on the patient's subsequent course (alive, mean follow-up of 27 months). The authors suggested that further evaluation of Thallium-201 and hexamethylpropyleneamine oxime (HMPAO), single-photon-emission computed tomography (SPECT) or magnetic resonance spectroscopy (MRS) was warranted. Dynamic susceptibility-weighted contrast-enhanced MRI has recently been suggested to improve prediction of tumor response after treatment for brain metastases and primary brain tumor.

The most appropriate frequency and type of follow-up after retreatment of a patient with brain metastases is a matter of debate. Given its wide availability in this country and superior sensitivity over computed tomography (CT), MRI is the preferred imaging modality. It is an expensive option, however, and its frequency of use should depend on the likelihood of obtaining useful information, not otherwise available, which could be acted upon for the patient's benefit.

A not uncommon problem after the treatment of brain metastases is the differentiation between tumor recurrence and radiation-induced scar tissue or necrosis. This is a particularly vexing problem in the patient who is asymptomatic and has a high performance status. F-18 deoxyglucose and methyl methionine PET scanning has been studied most and advocated for this purpose. When brain recurrence is confirmed, surgery and particularly radiosurgery may be useful in extending survival.

Summary

The issue of postirradiation management and retreatment thus revolves around three concerns. One is the need to assess the effects of and deal with any sequelae of treatment. Second is appropriate surveillance so that further treatment can be administered prior to symptoms when the patient may best tolerate additional treatment. The third is the goal of detecting recurrences when their size does not preclude the use of radiosurgery, arguably the most effective emerging option.

Abbreviations

- CT, computed tomography
- FDG-PET, fluorodeoxyglucose positron emission tomography
- KPS, Karnofsky Performance Status
- MRI, magnetic resonance imaging

- s/p, status-post
- SRS, stereotactic radiosurgery
- WBRT, whole brain radiotherapy

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate follow-up and retreatment of brain metastasis

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Simpson JR, Gaspar LE, Aref AM, Imperato JP, Marcus KJ, Rogers CL, Suh JH, Videtic GM, Wolfson AH, McDermott MW, Rogers L, Expert Panel on Radiation Oncology-Brain Metastases. Follow-up and retreatment of brain metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [23 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 (revised 2006)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology-Brain Metastases

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Joseph R. Simpson, MD; Laurie E. Gaspar, MD, MBA; Amr M. Aref, MD; Joseph P. Imperato, MD; Karen J. Marcus, MD; C. Leland Rogers, MD; John H. Suh, MD; Gregory M. Videtic, MD; Aaron H. Wolfson, MD; Michael W. McDermott, MD; Lisa Rogers, DO

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [American College of Radiology \(ACR\) Web site](#).

ACR Appropriateness Criteria® *Anytime, Anywhere*™ (PDA application). Available from the [ACR Web site](#).

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the [American College of Radiology \(ACR\) Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 30, 2001. The information was verified by the guideline developer as of February 20, 2001. This NGC summary was updated by ECRI Institute on May 16, 2007.

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